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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/810,682	03/29/2004	Michael Edward John Billingham	00042/US3	1241

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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 11/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/810,682	BILLINGHAM, MICHAEL EDWARD JOHN	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 27-32 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 27-32 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/674512.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. By Amendment filed September 15, 2006, claims 15-26 have been cancelled.

Applicants Response to Restriction Requirement Acknowledged

2. Applicant's election, without traverse, with the Group III, claims 27-32, is acknowledged. Accordingly, claims 27-32 are currently pending for prosecution on the merits of the case.

Priority

3. Acknowledgment is made of applicant's filing of this instant application as a continuation of US Application No. 10/146,919 filed May 17, 2002, abandoned, which is a continuation of 09/986,820 filed November 13, 2001, patented US Patent No. 6,414,026, which is a continuation of US Application No. 09/674,512 filed on November 16, 2000, patented US Patent No. 6,348,497, which is a 371 of PCT/GB99/01684 filed May 27, 1999.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 27-32 are rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The present claim is drawn to a method of alleviating complications from diabetes comprising administering an effective amount of compound of the formula (I).

It is generally recognized in the art that diabetes affects almost every system in the body and involves in pathologies of various diseases state including hyperosmolar coma, cerebral edema, myocardial infarction, mucormycosis, respiratory distress syndrome, vascular thrombosis, hypokalemia, infection, acute gastric dilatation or erosive edema, arteriosclerosis, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, diabetic foot ulcers, malignant external otitis, hypertriglyceridemia, necrobiosis lipoidica diabeticorum, hyperviscosity, obesity, leprechaunism, ataxia-telangiectasia, Rabson-Rendehall syndrome, Alstrom syndrome, Pineal hyperplasia syndrome, Werner syndrome and etc...

The specification discloses "accelerated cardiovascular problems associated with diabetes"(page 1, lines 9-10 of the instant specification) as the suitable of example fibrotic diseases that can be benefited from the administration of the claimed compound represented by the formula (I), which meets the written description. However, claim 1 is directed to encompass any "complications from diabetes", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. None of these meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. Mahurkar, 19 USPQ2d 1111, makes clear the "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of treating diabetes or the specific cardiovascular complications of diabetes, the skilled artisan cannot envision the claimed "complications from diabetes". Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for treating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966(1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989)* ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.*

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 27-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating diabetes or the specific cardiovascular complications of diabetes with a compound of formula (I), does not reasonably provide enablement for "complications of diabetes". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The instant claims are drawn to a method for alleviating "complications of diabetes" comprising administering a compound of formula (I).

The interpretation of the instant claims allows for the therapeutic treatment of various diseases state associated with diabetes including hyperosmolar coma, cerebral edema, myocardial infarction, mucormycosis, respiratory distress syndrome, vascular thrombosis,

hypokalemia, infection, acute gastric dilatation or erosive edema, arteriosclerosis, diabetic retinopathy, diabetic nephropathy, diabetic neuropathy, diabetic foot ulcers, malignant external otitis, hypertriglyceridemia, necrobiosis lipoidica diabeticorum, hyperviscosity, obesity, leprechaunism, ataxia-telangiectasia, Rabson-Rendehall syndrome, Alstrom syndrome, Pineal hyperplasia syndrome, Werner syndrome and etc.... (see "Diabetes Mellitus", Harrison's Principles of Internal Medicine, 12th Edition, 1991, pp. 1739-1759).

The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmacy art is high. The relative skill of those in the art of pharmaceuticals and the unpredictability of the pharmaceutical art is very high. In fact, the courts have made a distinction between mechanical elements function the same in different circumstances, yielding predictable results, chemical and biological compounds often react unpredictably under different circumstances. Nationwide Chem. Corp. v. Wright, 458 F. supp. 828, 839, 192 USPQ 95, 105(M.D. Fla. 1976); Aff'd 584 F.2d 714, 200 USPQ 257 (5th Cir. 1978); In re fischer, 427 F.2d 833, 839, 166 USPQ 10, 24(CCPA 1970). Thus, the physiological activity of a chemical or biological compound is considered to be an unpredictable art. For example, in Ex Parte Sudilovsky, the Court held that Appellant's invention directed to a method for preventing or treating a disease known as tardive dyskinesia using an angiotensin converting enzyme inhibitor involved unpredictable art because it concerned the pharmaceutical activity of the compound. 21 USPQ2d 1702, 1704-5(BDAI 1991); In re Fisher, 427 F.2d 1557, 1562, 29 USPQ, 22 (holding that the physiological activity of compositions of adrenocorticotropic hormones was unpredictable art; In re Wright, 9999 F.2d 1577, 1562, 29 USPQ d, 1570, 1513-14 (Fed. Cir. 1993) (holding that the physiological activity of RNA viruses was unpredictable art); Ex Parte

Hitzeman, 9 USPQ2d 1821, 1823 (BDAI 1987); Ex Parte Singh, 17 USPQ2d 1714, 1715, 1716 (BPAI 1990). Likewise, the physiological or pharmaceutical activity of alleviating complications of diabetes prior to filling of the instant invention was an unpredictable art.

The specification provides assays in vitro and vivo and demonstrates that said compound exhibits the activity in down regulating collagenase I and inhibit partially MMP promoter activity (Example). However, there is no demonstrated correlation that the tests and results apply to the claimed therapeutic utility embraced by the instant claims.

As discussed above, the claims are very broad due to the multitude diseases of that are described as being "complications of diabetes". Diabetes affects almost every system in the body and involves in pathologies of various diseases stated above. However, it is not known yet that a single underlying mechanism ties together all of the seemingly unrelated manifestations and the administration of single agent is effective against the unrelated manifestation encompassed by the instant claims. Therefore, the skilled artisan would turn to undue amount of trial and error to find out which disease or condition would be response to the administration of compounds of the formula (I).

As discussed in preceding comments, in the instant case, only limited number of disease is set forth, thereby failing to provide sufficient working examples. The instant claims read on any diseases associated with diabetes, necessitating an exhaustive search for the embodiments suitable to practice the claimed invention.

As discussed above, considering above factors, especially the "sufficient working examples", "the level of skill in the art", "the relative skill and the unpredictability in the pharmaceutical art" and "breadth of the claims", one having ordinary skill in the art would have

to undergo an undue amount of experimentation to practice the invention commensurate in scope with these claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 27-28, 30 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Edge et al. (US 4310544).

Edge teaches the use of the claimed compound of the formula (III) or its salt form for the treatment of atherosclerosis (column 5, lines 58-60).

Since the referenced atherosclerosis "metes and bounds" the broadly interpreted "complications from diabetes", Edge anticipates the claimed invention.

7. Claims 27-28, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Fitzgerald, J.D. (AN 1967:507356- Wien. Klin. Wochenschr., abstract, 1967, 79(39), pp. 716-20)

Fitzgerald teaches the use of compound of the formula (IV) for the treatment of cardiac infarction, hyperlipidemia with xanthomatosis and diabetic retinopathy.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claim 29 rejected under 35 U.S.C. 103(a) as being unpatentable over Edge et al. (US 4310544), and further in view of Leigh et al. (US 3549690).

The teaching of Edge has been discussed in above 35 USC 102(b) rejection.

Leigh teaches or suggests the hydroxyalkanoic acid derivatives, namely the compound of the formula II (α-[4-(p-chlorophenyl)benzyloxy]-α-methylpropionic acid where methyl substittuents on R1 and R2 position (abstract; column 1, lines 26-43; claims).

The teaching of Edge differs from the claimed invention in the use of compound of formula (II) where methyl substituents on R1 and R2 position.

One having ordinary skill in the art would have expected as taught by the combination (Edge and Leigh) that hydroxyalkanoic acid derivatives wherein R1 is alkyl radical (i.e., methyl or ethyl substituent) and R2 is alky radical (i.e., methyl or ethyl substituent) or phenyl radical would have similar activities as the compound of the formula III. One having ordinary skill in the art would have been motivated to employ the claimed compound represented by the formula (II) with the reasonable expectation of success that substitution of a methyl radical for ethyl

radical in R1 position and for phenyl in R2 position would not significantly alter the analogous properties of the compound of the reference due to close structural similarity of the compounds. See In re Grunwell, 203 USPQ 1055.

Conclusion

9. No Claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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